Radiation Oncology Review for Boards and MOC
Radiation Oncology
Review for Boards
and MOC

Editors

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To my parents without whom I would not have become the person that I am today

—Tithi Biswas

I would like to dedicate this book to my wife Melanie, my daughter Amelia, and my son Owen. Their continuing support has been instrumental in achieving my academic goals in radiation oncology and personal goals in life.

—George Rodrigues
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Preface

The continued practice of radiation oncology requires clinicians to integrate a variety of disciplines including basic science knowledge, clinical skills/practice, and treatment planning. As radiation oncology is an ever evolving field of medicine due to technological improvements and the generation of evidence, clinicians need various educational materials to keep up with practice changes.

Radiation Oncology Review for Boards and MOC was specifically written to efficiently review high-yield clinical concepts and knowledge for trainees studying for radiation oncology specific board examinations as well as established clinicians who need a quick review for maintenance of certification examinations. Ideally, this book should be used in concert with Radiation Oncology Primer and Review: Essential Concepts and Protocols (Rodrigues/Velker/Best, Demos Medical Publishing) in order to ensure a complete coverage of basic science concepts and treatment planning approaches.

Both the editorial team and individual authors were assembled for this book in order to provide a consistent presentation of clinical information to the reader. The book also contains end of chapter multiple choice questions with annotated answers to maximize learning for the reader. Two full practice tests (including annotated answers) on basic science, clinical science, and treatment-planning concepts covering both Radiation Oncology Review for Boards and MOC and Radiation Oncology Primer and Review: Essential Concepts and Protocols are included in this book to maximize the utility of covering this material prior to any board examination. Although pre-examination preparation is the main focus of the book, residents may also find the content of this review useful for teaching interactions and internal program examinations.

Ultimately, the primary goal of Radiation Oncology Review for Boards and MOC is to successfully prepare trainees or practicing clinicians for either primary board examinations or maintenance of certification examinations that are required for licensure in radiation oncology.

Finally, the authors would like to thank Rich Winters, David D’Addona, and Norman Graubart from Demos Publishing for their assistance and encouragement during the book writing and editing process.

Tithi Biswas, MD
George Rodrigues, MD, PhD, FRCPC
6.1 Nasopharynx

Epidemiology and Risk Factors

- There are only 5,000–6,000 new cases annually in the United States.
- It is more common in Southeast Asia, East Asia, Polynesia, North Africa, and for native peoples of the Arctic.
- Worldwide, there are 87,000 cases annually and 51,000 deaths from the disease.
- It is male-predominant.
- Median age at diagnosis is 55 years.
- Epstein Barr Virus (EBV) is the strongest risk factor for the nonkeratinizing, undifferentiated form (WHO type 2b).
  - EBV titer has also been shown to be prognostic.
- Alcohol and tobacco increase risk of developing the keratinizing squamous cell carcinoma form (WHO type I).

Anatomy and Patterns of Spread

- Boundaries of the nasopharynx: anterior—nasal cavity; posterior—clivus and C1–C2 vertebral body; superior—sphenoid sinus; inferior—soft palate.
- Most commonly arises in the pharyngeal recess just posterior to the torus tubarius (fossa of Rosenmüller).
- May also invade the sphenoid sinus and skull base → cavernous sinus.
- Named nerve palsies syndromes:
  - Jacod's: direct extension through foramen lacerum to cavernous Sinus (containing CN III, IV, V1, V2, V1) resulting in eye symptoms and upper face pain/anesthesia
  - St Villaret's: metastases to parapharyngeal space, or compression from nodes resulting in CN IX–XII AND sympathetic chain
  - Collet-Sicard: CN IX–XII involved
  - Vernet's (jugular foramen): CN IX–XI involved
  - Jackson's: CN X–XII involved.
- High propensity for lymphatic spread (70%–80%):
  - Nasopharynx cancer has highest risk of retropharyngeal and level V lymph node metastases

Presentation

- Most commonly presents with a neck mass from cervical nodal metastasis.
- Other presenting symptoms include otitis and hearing loss (Eustachian tube obstruction); nasal obstruction and epistaxis (anterior extension).
Other common presenting symptoms are: headaches, trismus, and nerve palsies (see anatomy and patterns of spread).

Differential diagnosis includes carcinoma, lymphoma, minor salivary gland tumor, plasmacytoma, melanoma, chordoma, rhabdomyosarcoma, and juvenile angiofibroma.

**Histology**

- **World Health Organization classification**
  - WHO type 1: keratinizing squamous cell carcinoma (20% of U.S. cases)
    - Keratinizing squamous cell carcinoma has highest risk for local failure and lowest risk for distant failure.
  - WHO type 2a: nonkeratinizing squamous cell carcinoma (uncommon)
  - WHO type 2b: undifferentiated carcinoma (99% of endemic cases)
    - Lymphoepithelioma: distinct entity with high lymphoid component. Easier to control locoregionally but equivalent survival due to higher rates of distant metastases.

**Diagnosis and Workup**

- History and physical exam including complete head and neck exam with fiberoptic nasopharyngolaryngoscopy and otoscopy
- Biopsy of suspicious lesions
- Routine laboratory studies. Consider EBV titer
- CT head/neck
- MRI skull base
- Chest X ray (CXR) for stage III/IV
- Consider PET/CT if stage III/IV (most will be)
- Dental evaluation, nutrition evaluation, speech and swallowing evaluation, and audiology testing
  - Consider prophylactic feeding tube placement in patients receiving chemoradiation

**Staging (AJCC 7th Edition)**

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tx</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor confined to the nasopharynx, or extends to oropharynx and/or nasal cavity without parapharyngeal extension*</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor with parapharyngeal extension*</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor involves bony structures of skull base and/or paranasal sinuses</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor with intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, or with extension to the infratemporal fossa/masticator space</td>
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</table>

<table>
<thead>
<tr>
<th>N-stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Unilateral metastasis in lymph node(s), 6 cm or less in greatest dimension, above the suprACLavicular fossa, and/or unilateral or bilateral, retropharyngeal lymph nodes, 6 cm or less, in greatest dimension†</td>
</tr>
<tr>
<td>N2</td>
<td>Bilateral metastasis in lymph node(s), 6 cm or less in greatest dimension, above the suprACLavicular fossa†</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in a lymph node(s)† greater than 6 cm and/or extension to suprACLavicular fossa</td>
</tr>
<tr>
<td>N3a</td>
<td>Greater than 6 cm in dimension</td>
</tr>
<tr>
<td>N3b</td>
<td>Extension to the suprACLavicular fossa</td>
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**M-stage**

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<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>I</td>
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<td>N0</td>
<td>M0</td>
</tr>
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<td>II</td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
</tr>
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<td></td>
<td>T2</td>
<td>N0–1</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
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<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N0–2</td>
<td>M0</td>
</tr>
<tr>
<td>IVA</td>
<td>T4</td>
<td>N0–3</td>
<td>M0</td>
</tr>
<tr>
<td>IVB</td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

* Parapharyngeal extension denotes posterolateral infiltration of tumor.
† Midline nodes are considered ipsilateral nodes.

**Treatment Overview**

- Stage I: Radiation therapy (RT) alone.
- Stages II to IVB: concurrent chemoradiation → adjuvant chemotherapy.
  - Concurrent chemotherapy: cisplatin 100 mg/m² q21 days × 3 cycles.
  - Adjuvant chemotherapy: cisplatin 80 mg/m² + 5-FU 1,000 mg/m² × 4 days q21 days × 3 cycles.
- Stage IVC: platinum-based combination chemotherapy → chemoradiation if complete response (CR).
- Recurrent disease: RT options include intensity modulated radiation therapy (IMRT), HDR brachytherapy or radiosurgery (30–50 Gy in 3–5 fractions show reasonable efficacy and safety).
- Consider salvage surgery if primary has less than CR or residual neck mass by imaging or physical examination at 6 to 12 weeks posttreatment.
- Toxicities:
  - Acute: fatigue, mucositis, xerostomia, dermatitis, nausea, dysphagia, odynophagia, and dysgeusia.
  - Late: soft tissue fibrosis, trismus, hearing loss, dysphagia, xerostomia, hypothyroidism, temporal lobe necrosis, osteoradionecrosis of skull base, delayed bulbar palsy, hypopituitarism, and RT-associated malignancy.

**Radiation Therapy Techniques**

- Simulation: supine, shoulder pulls, head, and shoulder mask
  - Wire lymph nodes
  - Mouthguards
- MRI and PET/CT fused for treatment planning
- Full-field simultaneous-integrated boost IMRT will be used to three target volumes treated over 33 fractions.
  - Gross tumor volume (GTV) will be gross primary disease and all nodes greater than 1 cm, with a necrotic center, or active on PET.
  - CTV70 will include a 5 mm expansion on GTV trimmed around critical structures. Planning target volume (PTV) will be an additional 5 mm expansion. Margin may be reduced when abutting critical structures such as the brainstem.
  - CTV59.4 will include CTV70 with a minimum 1 cm margin except when against critical structures. CTV59.4 will also include the entire nasopharynx, anterior 2/3 of clivus (all if involved), skull base covering foramen rotundum and foramen ovale, pterygoid fossa, pterygopalatine fossa, parapharyngeal space (to hyoid), inferior sphenoid sinus (all in T3/4 disease), posterior 1/3 of maxillary sinus/nasal...
cavity, cavernous sinus if T3/4 or bulky or involves roof of nasopharynx, bilateral retropharyngeal, and level IB-V lymph nodes.
- Bilateral IB lymph nodes can be spared if patient is node-negative.
  - CTV54 will include CTV59.4 and uninvolved low neck nodal regions.
- 95% of PTV receives prescription dose.
- No more than 5% of tissue outside of targets can receive 70 Gy.
- No more than 1 mL of unspecified tissue can receive 77 Gy or more.
- Organs at risk
  - Planning organ at risk volume (PRV)
    - Spinal cord + 5 mm
    - Brainstem + 1 mm
    - Optic apparatus + 1 mm
  - Brachial plexus: max 66 Gy
  - Mandible: max 70 Gy. If not possible, then V75 Gy less than 1 mL
  - Optic nerves/chiasm: max 50 Gy. PRV: max 54 Gy
  - Spinal cord: max 45 Gy. 1% PRV: max 50 Gy
  - Brainstem: max 54 Gy. PRV: max 60 Gy
  - Parotids: mean less than 26 Gy in at least one gland, or at least 50% of one gland less than 30 Gy
  - Glottic/supraglottic larynx: mean less than 37 Gy
  - Esophagus: mean less than 45 Gy
  - Cochlea: V55 Gy less than 5%

6.2 Oral Cavity

Epidemiology and Risk Factors
- There are approximately 30,000 new cases annually in the United States.
- It accounts for 30% of head and neck cancers.
- Subsites of oral cavity include: lips, oral tongue, floor of mouth, alveolar ridge, buccal mucosa, hard palate, and retromolar trigone.
- Distribution by subsite:

<table>
<thead>
<tr>
<th>Location</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Lips</td>
<td>45</td>
</tr>
<tr>
<td>Oral tongue</td>
<td>16</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>12</td>
</tr>
<tr>
<td>Alveolar ridge</td>
<td>12</td>
</tr>
<tr>
<td>Buccal mucosa</td>
<td>10</td>
</tr>
<tr>
<td>Hard palate</td>
<td>5</td>
</tr>
</tbody>
</table>

- Risk factors:
  - Alcohol and tobacco
  - Poor oral hygiene
  - Betel and areca nut chewing
  - UV radiation (lip)
  - Genetic predisposition: Plummer–Vinson syndrome, Fanconi’s anemia, Li Fraumeni syndrome
  - History of premalignant lesions (leukoplakia, erythroplakia)
- Oral cavity cancer carries extraordinary risk of metachronous primary cancers.
- Oral tongue cancers carry the worst prognosis of all oral cavity cancers.
Anatomy and Patterns of Spread

- Boundaries of the oral cavity: superior—hard palate, superior alveolar ridge, maxillary teeth; lateral—cheeks; posterior—anterior tonsillar pillars, circumvallate papillae; inferior—mylohyoid muscle, inferior alveolar ridge, teeth.
- Lymph node involvement is common.
  - Incidence of skip metastases for oral tongue lesions is approximately 15%.
  - Increasing depth of invasion, T-stage, and grade are associated with greater risk of lymph node involvement.
- Lymphatic drainage:
  - Upper lip: facial and level IB
  - Lower lip: I to III
  - Floor of mouth: I to III
  - Buccal mucosa: I to III
  - Alveolar ridge: levels I to III
  - Oral tongue: I to IV

Presentation

- Signs and symptoms:
  - Early: asymptomatic, slightly elevated red lesions with ill-defined borders, ill-fitting dentures
  - Late: ulcerated mass, pain, bleeding, difficulty with speech or swallowing secondary to tongue fixation, trismus, otalgia
- Referred otalgia:

<table>
<thead>
<tr>
<th>Cranial Nerve</th>
<th>Primary</th>
</tr>
</thead>
<tbody>
<tr>
<td>CN X (auricular (Arnold) nerve → postauricular)</td>
<td>Larynx, hypopharynx</td>
</tr>
<tr>
<td>CN IX (nerve of Jacobson → tympanic cavity)</td>
<td>Base of tongue</td>
</tr>
<tr>
<td>CN V₃ (auriculotemporal nerve → preauricular)</td>
<td>Oral tongue</td>
</tr>
</tbody>
</table>

Histology

- 95% are squamous cell carcinomas.
- Other histologies include: minor salivary gland tumors greater than melanoma, ameloblastoma, lymphoma, sarcoma, and plasmacytoma.

Diagnosis and Workup

- History and physical exam including complete head and neck exam with careful inspection and palpation of oral cavity and anterior oropharynx, fiberoptic nasopharyngolaryngoscopy, and palpation of all neck levels
- Biopsy of lesion
- CT head/neck if greater than T1
- CXR for stages III/IV
- Consider PET/CT and MRI
- Routine laboratory studies
- Dental evaluation, nutrition evaluation, speech and swallowing evaluation, and audiology testing
  - Consider prophylactic feeding tube placement in patients receiving chemoradiation.
### Staging (AJCC 7th Edition)

#### T-stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T&lt;sub&gt;x&lt;/sub&gt;</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor greater than 2 cm but not more than 4 cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor more than 4 cm in greatest dimension</td>
</tr>
<tr>
<td>T4a</td>
<td>Moderately advanced local disease</td>
</tr>
<tr>
<td></td>
<td>(lip) Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face, that is, chin or nose</td>
</tr>
<tr>
<td></td>
<td>(oral cavity) Tumor invades adjacent structures only (e.g., through cortical bone, mandible or maxilla) into deep [extrinsic] muscle of tongue [genioglossus, hyoglossus, palatoglossus, and styloglossus], maxillary sinus, skin of face</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery</td>
</tr>
</tbody>
</table>

Note: Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify a tumor as T4.

#### N-stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension</td>
</tr>
<tr>
<td>N2a</td>
<td>Metastasis in single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N2b</td>
<td>Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N2c</td>
<td>Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in a lymph node more than 6 cm in greatest dimension</td>
</tr>
</tbody>
</table>

#### M-stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastases</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>

#### Group Stage

<table>
<thead>
<tr>
<th>Group</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>II</td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N0–1</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
<td>T1–2</td>
<td>N2</td>
<td>M0</td>
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<td></td>
<td>T3</td>
<td>N0–2</td>
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<tr>
<td>IVA</td>
<td>T4</td>
<td>N0–3</td>
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<tr>
<td>IVB</td>
<td>Any T</td>
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<td>M0</td>
</tr>
<tr>
<td>IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
Treatment Overview

- Lip
  - Stages I to II: Surgery or RT.
  - Stages III to IVB: Prefer surgery with neck dissection; alternative is chemoradiation.
    - Preferred concurrent chemotherapy: cisplatin 100 mg/m² q21 days × 3 cycles.
  - Notes
    - Re-excite if feasible for positive surgical margin.
    - Postoperative RT indicated for T3/T4, close margin, greater than 1 LN involved, perineural invasion (PNI), Lympho vascular space invasion (LVSI), or level IV to V lymph node involvement.
    - Postoperative chemoradiation indicated for positive margin or extracapsular extension.
    - Consider salvage surgery if primary has less than CR or residual neck mass by imaging or physical examination at 6 to 12 weeks posttreatment.

- Oral cavity
  - Stages I to II: Surgery or RT.
  - Stage III (T3N0): Surgery.
  - Stages III (T3N1)–IVB: Surgery.
  - Unresectable: Chemoradiation
    - Preferred concurrent chemotherapy: cisplatin 100 mg/m² q21 days × 3 cycles.
  - Notes:
    - Re-excite if feasible for positive surgical margin.
    - Neck dissection—supraomohyoid dissection, levels I to III.
    - Elective neck dissection based on depth of invasion: if greater than 4 mm elective dissection should be strongly considered if RT is not planned. If less than 2 mm, elective dissection is indicated only in highly selective situations. If 2 to 4 mm, clinical judgement should be utilized (as to reliability of follow-up, etc.).
    - Postoperative RT indicated for T3/T4, close margin, greater than 1 LN involved, PNI, LVSI, or level IV–V lymph node involvement.
    - Postoperative chemoradiation indicated for positive margin or extracapsular extension.
    - Consider salvage surgery if primary has less than CR or residual neck mass by imaging or physical examination at 6 to 12 weeks posttreatment.

- Toxicities
  - Acute: fatigue, mucositis, xerostomia, dermatitis, nausea, dysphagia, odynophagia, and dysgeusia.
  - Late: pharyngocutaneous fistula, soft tissue fibrosis, dysphagia, xerostomia, hypothyroidism, osteoradionecrosis, and RT-associated malignancy.

Radiation Therapy Techniques

- Simulation: supine, shoulder pulls, head and shoulder mask
  - Wire lymph nodes, surgical scars, oral commissure
  - Bite block
  - Mouthguards
- Preoperative diagnostic imaging fused for treatment planning
- Full field simultaneous-integrated-boost IMRT will be used to target volumes.
  - Alternative techniques include split-field IMRT (match line just above arytenoids), sequential boost, brachytherapy boost, and 3D-conformal planning.
- Postoperative RT:
  - 60 Gy to high-risk areas and postoperative bed.
  - 54 Gy to intermediate-risk areas outside of operative bed and elective neck.
  - Consider 66 Gy for areas at very high risk (extra capsular extension [ECE], positive margin).
- Definitive RT:
  - GTV (for unresectable disease) will be gross primary disease and all nodes greater than 1 cm or with a necrotic center or active on PET.
Head and Neck Malignancies

PTV70 will be a 3 to 5 mm expansion on GTV.
- 60 to 66 Gy sufficient for T1 tumors.
- 66 to 70 Gy sufficient for T2 tumors.
- CTV63 will include GTV with a minimum 1 cm margin except when against critical structures and high-risk neck.
- CTV56 will include intermediate-risk areas and elective neck.
- Other RT options include: brachytherapy alone (LDR or HDR) or EBRT (50 Gy) + brachytherapy (16 Gy).

Lips
- Small lesions can be treated orthovoltage photons, electrons, or brachytherapy.
  - Consider bolus for superficial lesions, lead cutout, and lead shield to protect oral cavity and mandible.
- Upper lesions: consider covering perifacial lymphatics for advanced tumors.

Oral tongue, floor of mouth
- Small lesions can be treated with brachytherapy.
- Bite block and mouthguards

Buccal mucosa
- Wire oral commissures
- Bite block and mouthguards

Alveolar ridge, hard palate, and retromolar trigone
- EBRT preferred to brachytherapy due to risk of osteoradionecrosis.
- Bite block and mouthguards

Organs at risk
- Spinal cord: max 45 Gy
- Brainstem: max 54 Gy
- Parotids: combined mean less than 26 Gy, or mean less than 20 Gy in at least one gland
- Glottic/supraglottic larynx: mean less than 37 Gy
- Mandible: max 70 Gy

6.3 Oropharynx

Epidemiology and Risk Factors
- There are approximately 8,500 new cases of oropharynx cancer annually in the United States.
- Rising incidence occurs in middle-aged White males without alcohol or tobacco history.
- Subsites of oropharynx include: base of tongue, soft palate, palatine tonsils, tonsillar pillars, and lateral and posterior pharyngeal walls between nasopharynx and pharyngoepiglottic fold.
- Risk factors:
  - HPV 16, 18, 31 infection
  - Alcohol and tobacco
  - Betel and areca nut chewing
- Risk of second primary cancers is very high (25%), especially in patients who continue to smoke.
- Risk stratification groups from RTOG 0129:
  - Low Risk: p16+, no smoking history less than 10 pack years
    - 3yr OS 94%
  - Intermediate Risk: p16+ with smoking history less than 10 pack years, or p16– and no smoking history (<10 pack years)
    - 3yr OS 67%
  - High Risk: p16- with smoking history greater than 10 pack years
    - 3yr OS 42%
**Anatomy and Patterns of Spread**

- Oropharynx bounded by soft palate superiorly, pharyngeal walls laterally, pharyngeal wall posteriorly, and hyoid bone inferiorly.
- Lymphatic drainage generally extensive: upper jugulodigastric, bilateral cervical, and retropharyngeal lymph nodes.
- Clinical nodal involvement at diagnosis:
  - BOT: 75%
  - Tonsillar fossa: 75%
  - Tonsillar pillar: 45%
  - Soft palate: 45%
  - Oropharyngeal wall: 70%

**Presentation**

- Most common presenting symptom is a neck mass.
- Other symptoms on presentation include a mucosal lesion with pain and bleeding, sore throat, dysphagia, globus sensation, referred otalgia, hoarse voice, poor articulation from fixed tumor, foul breath from ulceration and necrosis, trismus, and temporal pain.
- Referred otalgia

<table>
<thead>
<tr>
<th>Cranial Nerve</th>
<th>Primary</th>
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<tbody>
<tr>
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<td>Larynx, hypopharynx</td>
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<td>Base of tongue</td>
</tr>
<tr>
<td>CN V₃ (auriculotemporal nerve → preauricular)</td>
<td>Oral tongue</td>
</tr>
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</table>

**Histology**

- 95% are squamous cell carcinoma.
- Other histologies include: non-Hodgkin's lymphoma, lymphoepithelioma, adenoid cystic carcinoma, mucoepidermoid carcinoma, adenocarcinoma, verrucous carcinoma, plasmacytoma, melanoma, and small-cell carcinoma.

**Diagnosis and Workup**

- History and physical exam including complete head and neck exam with careful inspection and palpation of oral cavity and anterior oropharynx, fiberoptic nasopharyngolaryngoscopy, and palpation of all neck levels
- Panendoscopy
- Biopsy of lesion
  - Perform HPV testing
- CT head/neck if greater than T1
- CXR for stages III/IV
- Consider PET/CT and MRI
- Routine laboratory studies
- Dental evaluation, nutrition evaluation, speech and swallowing evaluation, and audiology testing
  - Consider prophylactic feeding tube placement in patients receiving chemoradiation
## Staging (AJCC 7th Edition)

### T-stage

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Tx</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor more than 2 cm but not more than 4 cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor more than 4 cm in greatest dimension or extension to lingual surface of epiglottis</td>
</tr>
<tr>
<td>T4a</td>
<td>Moderately advanced local disease. Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible*</td>
</tr>
<tr>
<td>T4b</td>
<td>Very advanced local disease. Tumor invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases carotid artery</td>
</tr>
</tbody>
</table>

* Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of larynx.

### N-stage

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<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension</td>
</tr>
<tr>
<td>N2a</td>
<td>Metastasis in single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N2b</td>
<td>Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N2c</td>
<td>Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in a lymph node more than 6 cm in greatest dimension</td>
</tr>
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</table>

### M-stage

<table>
<thead>
<tr>
<th>M-stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastases</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>

### Group Stage

<table>
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<th>M-stage</th>
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</tr>
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</tr>
<tr>
<td>III</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1–3</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>IVA</td>
<td>T4a</td>
<td>N0–1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1–4a</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>IVB</td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>Any N</td>
<td>M0</td>
</tr>
<tr>
<td>IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
Treatment Overview

- T1–2, N0–1: RT or surgery ± neck dissection
  - Consider chemoradiation for T2N1
- T3–4a, N0–1: Concurrent chemoradiation (preferred) or surgery
- Any T, N2–3: Concurrent chemoradiation (preferred) or surgery
- T4b, any N, or unresectable: Concurrent chemoradiation
- Notes:
  - Preferred concurrent chemotherapy: cisplatin 100 mg/m² q21 days × 3 cycles.
  - Postoperative RT indicated for T3/T4, close margin, N2 or N3 disease, PNI, LVSI, or level IV to V lymph node involvement.
  - Postoperative chemoradiation indicated for positive margin or extracapsular extension.
  - Consider salvage surgery if primary has less than CR or residual neck mass by imaging or physical examination at 6 to 12 weeks posttreatment.

Radiation Therapy Techniques

- Simulation: supine, shoulder pulls, head and shoulder mask
  - Wire lymph nodes, surgical scars
  - Bite block
  - Mouthguards
- Preoperative diagnostic imaging fused for treatment planning
- Full field simultaneous-integrated-boost IMRT used to target volumes
  - Alternative techniques include split-field IMRT (match line just above arytenoids), sequential boost, brachytherapy boost, and 3D-conformal planning.
    - Split-field IMRT technique matched to a supraclavicular AP field with a half-beam block ONLY when there is no gross disease at the level of the arytenoids.
- Postoperative RT:
  - 60 Gy to tumor bed + ~1 cm margin.
  - 57 Gy to entire primary operative bed and involved neck nodal levels.
  - 54 Gy to intermediate-risk areas outside of operative bed and elective neck.
  - Consider 66 Gy for areas at very high risk (ECE, positive margin).
- Definitive RT:
  - GTV (for unresectable disease) will be gross primary disease and all nodes greater than 1 cm or with a necrotic center or active on PET.
  - PTV70 will be a 3–5 mm expansion on GTV.
    - 60 to 66 Gy sufficient for T1 tumors.
    - 66 to 70 Gy sufficient for T2 tumors.
  - CTV63 will include GTV with a minimum 1 cm margin except when against critical structures and high-risk neck.
  - CTV56 will include intermediate-risk areas and elective neck.
- Notes:
  - In general, treat bilateral neck (retropharyngeals, levels II–IV).
  - If more anterior tumor, consider treating level IB lymph nodes.
  - If tonsil primary with greater than 1 cm extension invasion into soft palate or base of tongue and N1–2a, treat ipsilateral neck only.
  - Treat ipsilateral IB if level II involved.
  - Treat ipsilateral level V for T3+ or N+.
- Organs at risk:
  - Spinal cord: max 45 Gy
  - Brainstem: max 54 Gy
  - Oral cavity: no hot spots
6.4 Hypopharynx

Epidemiology and Risk Factors

- There are approximately 3,000 new cases of hypopharynx cancer annually in the United States.
- Subsites of hypopharynx include: pyriform sinuses (most common), posterior pharyngeal walls, and postcricoid area (least common).
- Risk factors:
  - Alcohol and tobacco
  - Betel and areca nut chewing
  - Iron, vitamin C, vitamin B12, and vitamin C deficiencies

Anatomy and Patterns of Spread

- Hypopharynx is pharynx from hyoid bone to bottom of cricoid.
- Lymph node drainage: usually to levels II to V, retropharyngeals, paratracheal, paraesophageal
  - Low neck (level IV) lymph node involvement has a worse prognosis.
- Risk of lymph node involvement is 60% for early-stage disease and 85% for advanced-stage disease.

Presentation

- Typical presentation includes sore throat, otalgia, hoarse voice, dysphagia, odynophagia, and trismus.
- Referred otalgia

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Histology

- 95% are squamous cell carcinoma.

Diagnosis and Workup

- History and physical exam including complete head and neck exam with careful inspection and palpation of oral cavity and anterior oropharynx, fiberoptic nasopharyngolaryngoscopy, and palpation of all neck levels
- Panendoscopy
- Bronchoscopy if clinically indicated
- Biopsy of lesion
- CT head/neck
- CXR for stage III/IV
- Consider PET/CT and MRI
- Routine laboratory studies
- Dental evaluation, nutrition evaluation, speech and swallowing evaluation, and audiology testing
  - Consider prophylactic feeding tube placement in patients receiving chemoradiation
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<td>Tumor limited to one subsite of hypopharynx and/or 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades more than one subsite of hypopharynx or an adjacent site, or measures more than 2 cm but not more than 4 cm in greatest dimension without fixation of hemilarynx</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor more than 4 cm in greatest dimension or with fixation of hemilarynx or extension to esophagus</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, or central compartment soft tissue†</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures</td>
</tr>
</tbody>
</table>

† Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.

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<tr>
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<th>T</th>
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<th>M</th>
</tr>
</thead>
<tbody>
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<td>Tis</td>
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</tr>
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</tr>
<tr>
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<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>T1–3</td>
<td></td>
<td>N1</td>
<td>M0</td>
</tr>
</tbody>
</table>

*(continued)*
Treatment Overview

- Most T1, N0; selected T2, N0 (not requiring total laryngectomy): RT or surgery.
  - Surgery is partial laryngopharyngectomy with neck dissection.
- T1, N+; T2–3, any N (requiring total laryngectomy): Induction chemotherapy → RT or chemoradiation (if complete or partial response) or surgery (if less than partial response) OR concurrent chemoradiation OR surgery.
  - Surgery is laryngopharyngectomy with neck dissection.
- T4a, any N (requiring total laryngectomy): surgery (preferred) OR induction chemotherapy → RT or chemoradiation (if complete or partial response) or surgery (if less than partial response) OR concurrent chemoradiation.
- T4b, any N, or unresectable
  - Concurrent chemoradiation
- Notes:
  - Induction chemotherapy: docetaxel, cisplatin, 5-FU.
    - If complete response or partial response at primary site and stable or improved disease in neck: chemoradiation
    - If less than partial response at primary site or progression in neck: salvage surgery
  - Following induction, concurrent chemotherapy: weekly platinum, weekly taxanes, or cetuximab.
  - Preferred concurrent chemotherapy without induction chemotherapy: cisplatin 100 mg/m² q21 days × 3 cycles.
  - Postoperative RT indicated for T3/T4, close margin, N2 or N3 disease, PNI, LVSI, or level IV–V lymph node involvement.
  - Postoperative chemoradiation indicated for positive margin or extracapsular extension.
  - Consider salvage surgery if primary has less than CR or residual neck mass by imaging or physical examination at 6 to 12 weeks posttreatment.

Radiation Therapy Techniques

- Simulation: supine, shoulder pulls, head and shoulder mask
  - Wire lymph nodes, surgical scars
  - Mouthguards
- Preoperative diagnostic imaging fused for treatment planning
- Full field simultaneous-integrated-boost IMRT will be used to target volumes.
  - Alternative techniques include split-field IMRT (match line just above arytenoids), sequential boost, brachytherapy boost, and 3D-conformal planning.
- Postoperative RT:
  - 60 Gy to high-risk areas and postoperative bed.
  - 54 Gy to intermediate-risk areas outside of operative bed and elective neck.
  - Consider 66 Gy for areas at very high risk (ECE, positive margin).
Definitive RT:
- GTV (for unresectable disease) will be gross primary disease and all nodes greater than 1 cm or with a necrotic center or active on PET.
- PTV70 will be a 3 to 5 mm expansion on GTV.
  - 60 to 66 Gy sufficient for T1 tumors.
  - 66 to 70 Gy sufficient for T2 tumors.
- CTV63 will include GTV with a minimum 1 cm margin except when against critical structures and high-risk neck.
- CTV56 will include intermediate-risk areas and elective neck.

Notes:
- Treat bilateral neck (retropharyngeals, levels II–V) in all cases.
- Boost tracheal stoma to 60 to 66 Gy if: emergent tracheostomy, subglottic extension, soft tissue invasion, ECE in level VI, scar crosses stoma, or close/positive margin.

Organs at risk:
- Spinal cord: max 45 Gy
- Brainstem: max 54 Gy
- Brachial plexus: max 66 Gy
- Oral cavity: no hot spots
- Parotids: combined mean less than 26 Gy, or mean less than 20 Gy in at least one gland
- Mandible: max 70 Gy

6.5 Larynx

Epidemiology and Risk Factors
- There are approximately 13,000 new cases of larynx cancer annually in the United States and 3,600 cancer-related deaths annually.
- 2/3 are glottic, 1/3 are supraglottic, 2% are subglottic.
- It is more common in men.
- Synchronous primaries in aerodigestive tract up to 5%.
- Risk factors:
  - Alcohol and tobacco
  - Occupation based on voice

Anatomy and Patterns of Spread
- Subsites:
  - Supraglottis:
    - Epiglottis
    - Aryepiglottic folds
    - False cords
    - Ventricles
    - Arytenoids
  - Glottis:
    - True vocal cords
    - Anterior commissure
  - Subglottis:
    - 5 mm below true vocal cords to bottom of cricoid
- Lymph node drainage:
  - Supraglottis:
    - 55% are node positive at diagnosis
    - Levels II to IV most commonly involved
Glottis:
- Less than 1% of T1 tumors, 2% to 5% of T2, and 20% to 30% of T3 to 4 are node positive at diagnosis
- Levels II to IV most commonly involved

Subglottis:
- Pretracheal (Delphian), paratracheal, and inferior jugular most commonly involved

Presentation
- Presentation:
  - Supraglottis: dysphagia, odynophagia, persistent sore throat, otalgia
  - Glottis: hoarse voice, persistent sore throat
  - Subglottis: stridor, dyspnea
- Referred otalgia:

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</table>

Histology
- 95% are squamous cell carcinomas.
  - Verrucous carcinoma (1%–2%) is a variant that is low grade, infrequently metastasizes, and may undergo anaplastic transformation after RT (controversial). Surgery preferred.
- Other histologies include: minor salivary gland carcinomas, lymphoma, plasmacytoma, carcinoid, sarcoma, melanoma.

Diagnosis and Workup
- History and physical exam including complete head and neck exam with fiberoptic nasopharyngolaryngoscopy
  - Consider videostroboscopy for functional evaluation and documentation of baseline tumor characteristics and vocal cord function.
- Biopsy of suspicious lesions
- Panendoscopy
- CT head and neck
- Consider MRI
- Consider PET/CT for stage III/IV disease
- Chest x-ray
- Pulmonary function tests for surgery candidates
- Dental evaluation, nutrition evaluation, speech and swallowing evaluation, and audiology testing
  - Consider prophylactic feeding tube placement in patients receiving chemoradiation.

Staging (AJCC 7th Edition)

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tx</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
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</table>

(continued)
### T-stage

#### Supraglottis

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor limited to one subsite of supraglottis with normal vocal cord mobility</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor limited to larynx with vocal cord fixation and/or invades any of the following postcricoid area, preepiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures</td>
</tr>
</tbody>
</table>

#### Glottis

<table>
<thead>
<tr>
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<th>Description</th>
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<tbody>
<tr>
<td>T1a</td>
<td>Tumor limited to one vocal cord</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumor involves both vocal cords</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor limited to the larynx with vocal cord fixation and/or invasion of paraglottic space, and/or inner cortex of the thyroid cartilage</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures</td>
</tr>
</tbody>
</table>

#### Subglottis

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor limited to the subglottis</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor extends to vocal cord(s) with normal or impaired mobility</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor limited to larynx with vocal cord fixation</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures</td>
</tr>
</tbody>
</table>

#### N-stage

<table>
<thead>
<tr>
<th>N-stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension</td>
</tr>
<tr>
<td>N2a</td>
<td>Metastasis in single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N2b</td>
<td>Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
</tbody>
</table>

(continued)
Treatment Overview

- **Glottic:**
  - Tis: Endoscopic resection (preferred) or RT
  - T1–2N0, select T3 N0 (amenable to larynx preservation): Primary RT or partial laryngectomy
  - T3, Any N (requiring total laryngectomy): Chemoradiation or total laryngectomy
  - T4a, Any N: Total laryngectomy (preferred) or chemoradiation
  - T4b, Any N: Chemoradiation

- **Supraglottic:**
  - Amenable to larynx preservation:
    - T1–2N0, selected T3: Endoscopic resection or partial supraglottic laryngectomy or definitive RT
    - T1–2N+, selected T3N1: Partial supraglottic laryngectomy or chemoradiation or radiation
  - Requiring total laryngectomy:
    - T3N0: Laryngectomy or chemoradiation
    - T3N2–3: Laryngectomy or chemoradiation
  - T4a, Any N: Laryngectomy + RT or chemoradiation
  - T4b, Any N or unresectable: Chemoradiation

- **Subglottic:**
  - Total laryngectomy + postoperative RT preferred
  - Primary chemoradiation may be considered
• Notes:
  o Re-excite if feasible for positive surgical margin.
  o Postoperative RT indicated for T3/T4, close margin, greater than 1 LN involved, PNI, LVSI, soft tissue invasion, emergent trach.
  o Postoperative chemoradiation indicated for positive margin or extracapsular extension.
  o Consider salvage surgery if primary has less than CR or residual neck mass by imaging or physical examination at 6 to 12 weeks posttreatment.
  o Induction chemotherapy can be considered for T3 and node positive cases:
    ■ Complete response at primary site: definitive RT
    ■ Partial response at primary site: definitive RT or chemoradiation
    ■ Less than partial response at primary site: surgery

**Radiation Therapy Techniques**

• Early glottic (T1 to 2N0):
  o Simulation: supine, shoulder pulls, neck extension, head and shoulder mask
  o Opposed lateral fields (5 cm × 5 cm or 6 cm × 6 cm), 4 to 6 MV photons, wedges
    ■ Superior border: thyroid notch
    ■ Inferior border: bottom of cricoid (about C6)
    ■ Posterior: anterior aspect of vertebral bodies
    ■ Anterior: flash skin
  o Dose
    ■ Tis: 66 Gy in 33 fractions or 60.75 Gy in 27 fractions
    ■ T1: 66 Gy in 33 fractions or 63 Gy in 28 fractions
    ■ T2: 70 Gy in 35 fractions (6 fractions per week) or 65.25 Gy in 29 fractions
  o Note: Keep total treatment time to less than 6 weeks.

• Advanced larynx:
  o Simulation: supine, shoulder pulls, head and shoulder mask
  o Wire lymph nodes, surgical scars
  o Preoperative diagnostic imaging fused for treatment planning
  o Full field simultaneous-integrated-boost IMRT will be used to target volumes
  o Postoperative RT:
    ■ 60 Gy to high-risk areas and postoperative bed
    ■ 54 Gy to intermediate-risk areas outside of operative bed and elective neck
    ■ Consider 66 Gy for areas at very high risk (ECE, positive margin)
  o Definitive RT:
    ■ GTV (for unresectable disease) will be gross primary disease and all nodes greater than 1 cm or with a necrotic center or active on PET.
    ■ PTV70 will include GTV plus 3 to 5 mm margin.
    ■ CTV63 will include GTV with a minimum 1 cm margin except when against critical structures and high-risk neck.
    ■ CTV56 will include intermediate-risk areas and elective neck.
    ■ *Consider altered fractionation for radiation alone.
  o Notes:
    ■ Except for early stage glottis cancers, treat bilateral neck (levels II–IV).
    ■ Boost tracheal stoma to 60 to 66 Gy if: emergent tracheostomy, subglottic extension, soft tissue invasion, ECE in level VI, scar crosses stoma, or close/positive margin.
  o Organs at risk:
    ■ Brachial plexus max dose 66 Gy
    ■ Mandible 70 Gy; if not possible, then V75 Gy <1 mL
    ■ Spinal cord max 45 Gy; 1% PRV max 50 Gy
    ■ Brainstem max 54 Gy; PRV max 60 Gy
- Parotids mean dose less than 26 in at least one, or at least 50% of one gland less than 30 Gy
- Esophagus mean dose less than 45 Gy

6.6 Thyroid

Epidemiology and Risk Factors

- Thyroid tumors are the most common endocrine neoplasms.
- There are approximately 30,000 new cases annually in the United States.
- Papillary and follicular histologies are more than twice as common in women than in men.
- Risk factors:
  - Prior ionizing radiation exposure
  - Dietary iodine content
  - Family history of thyroid cancer:
    - Multiple endocrine neoplasia type 2 (MEN-2)—medullary thyroid cancer
    - Cowden’s syndrome—papillary thyroid cancer
    - Gardner’s syndrome—papillary thyroid cancer

Anatomy and Patterns of Spread

- Most is commonly spread locally, with extrathyroidal invasion of soft tissue.
- Nodal involvement is common (central compartment, tracheo-esophageal groove, Delphian nodes, cervical nodes, superior mediastinum greater than supraclavicular, retropharyngeal).
- Superior mediastinal nodal involvement is usually associated with extensive neck nodal involvement.
- Common sites for distant metastatic disease include lung and bone.

Presentation

- Typically presents as palpable anterior neck nodule.
- Advanced disease can present with hoarseness from recurrent laryngeal nerve paralysis, breathing, or swallowing difficulties.

Histology

- Most thyroid nodules are benign.
- Pathology:
  - Papillary thyroid cancer accounts for 40% to 90% cases, usually younger women.
  - Follicular thyroid cancer (includes oxyphilic or Hurthle cell variants) accounts for 15% to 40% cases.
  - Medullary thyroid cancer accounts for 2% to 8% cases.
  - Anaplastic thyroid cancer accounts for 1% to 5% cases.
  - Other histologies include sarcomas, malignant hemangioendotheliomas, and lymphomas.

Diagnosis and Workup

- History and physical
- Thyroid ultrasound
- CT neck
  - Avoid iodinated contrast as this will block treatment with I-131 for approximately 6 months.
- Fine needle aspiration biopsy
- Chest x-ray
- Consider preoperative vocal cord examination; if vocal cord paralysis suspected from pressure or invasion of recurrent laryngeal nerve
• Labs including TSH, T3, T4, thyroglobulin
  o For medullary carcinoma, check calcitonin, calcium, CEA, and urine and serum catecholamines.
• Postoperative whole body RAI scan (papillary and follicular thyroid cancer)
• Age, histology, and anatomic extent of disease are of prognostic importance.

**Staging (AJCC 7th Edition)**

<table>
<thead>
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<tbody>
<tr>
<td><strong>Tx</strong></td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td><strong>T0</strong></td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td><strong>T1a</strong></td>
<td>Tumor 1 cm or less, limited to the thyroid</td>
</tr>
<tr>
<td><strong>T1b</strong></td>
<td>Tumor more than 1 cm but not more than 2 cm, limited to the thyroid</td>
</tr>
<tr>
<td><strong>T2</strong></td>
<td>Tumor more than 2 cm but not more than 4 cm, limited to the thyroid</td>
</tr>
<tr>
<td><strong>T3</strong></td>
<td>Tumor more than 4 cm in greatest dimension limited to the thyroid, or any tumor with minimal extrathyroid extension</td>
</tr>
<tr>
<td><strong>T4a</strong></td>
<td>Tumor of any size extending beyond the thyroid capsule to invade subcutaneous tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve</td>
</tr>
<tr>
<td><strong>T4b</strong></td>
<td>Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels</td>
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<table>
<thead>
<tr>
<th>N-stage</th>
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</thead>
<tbody>
<tr>
<td><strong>N0</strong></td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td><strong>N1a</strong></td>
<td>Metastasis to level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes) Regional lymph node metastasis</td>
</tr>
<tr>
<td><strong>N1b</strong></td>
<td>Metastasis to unilateral, bilateral, or contralateral cervical (Levels I–V) or retropharyngeal or superior mediastinal lymph nodes (Level VII)</td>
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<thead>
<tr>
<th>M-stage</th>
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<tbody>
<tr>
<td><strong>M0</strong></td>
<td>No distant metastases</td>
</tr>
<tr>
<td><strong>M1</strong></td>
<td>Distant metastases</td>
</tr>
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* All anaplastic carcinomas are considered T4 tumor:
  • T4a: Intrathyroidal anaplastic carcinoma
  • T4b: Anaplastic carcinoma with gross extrathyroid extension

**Group Stage**

**Papillary or Follicular (Differentiated) UNDER 45 YEARS**

<table>
<thead>
<tr>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Any T</td>
<td>Any N</td>
</tr>
<tr>
<td>II</td>
<td>Any T</td>
<td>Any N</td>
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(continued)
Group Stage

Papillary or Follicular (Differentiated) 45 YEARS AND OLDER

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<thead>
<tr>
<th>T</th>
<th>N</th>
<th>M</th>
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<tbody>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
</tr>
<tr>
<td>II</td>
<td>T2</td>
<td>N0</td>
</tr>
<tr>
<td>III</td>
<td>T3</td>
<td>N0</td>
</tr>
<tr>
<td></td>
<td>T1–3</td>
<td>N1a</td>
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<tr>
<td>IVA</td>
<td>T4a</td>
<td>N0–1b</td>
</tr>
<tr>
<td></td>
<td>T1–3</td>
<td>N1a</td>
</tr>
<tr>
<td>IVB</td>
<td>T4b</td>
<td>Any N</td>
</tr>
<tr>
<td>IVC</td>
<td>Any T</td>
<td>Any N</td>
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Medullary Carcinoma

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<th>M</th>
</tr>
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<td>II</td>
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<td>N0</td>
</tr>
<tr>
<td>III</td>
<td>T1–3</td>
<td>N1a</td>
</tr>
<tr>
<td>IVA</td>
<td>T4a</td>
<td>N0–1b</td>
</tr>
<tr>
<td></td>
<td>T1–3</td>
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<td>Any N</td>
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Anaplastic Carcinoma

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<tbody>
<tr>
<td>IVA</td>
<td>T4a</td>
<td>Any N</td>
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<tr>
<td>IVB</td>
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<td>Any N</td>
</tr>
<tr>
<td>IVC</td>
<td>Any T</td>
<td>Any N</td>
</tr>
</tbody>
</table>

Treatment Overview

- Surgery is the standard primary treatment.
- Extent of initial surgery is controversial, ranging from ipsilateral thyroid lobectomy to total thyroidectomy.
- Extent of neck node removal is controversial.
  - Role of prophylactic or prognostic lymph node dissections is unclear.
  - Modified radical neck dissection is indicated for gross nodal metastases.
- Thyroxine-suppressive therapy of TSH is standard postoperative management for papillary and follicular thyroid cancers.
- Radioactive iodine therapy is used for most follicular thyroid carcinoma, unresectable or residual papillary thyroid carcinoma, and distant metastatic disease.
EBRT is considered for patients with locally advanced disease with high-risk surgical pathologic features (close/positive margins, extrathyroidal invasion, multiple nodes involved), recurrent or metastatic disease nonresponsive to RAI.

For differentiated thyroid cancers, role of chemotherapy is limited; doxorubicin is the most active single agent.

For anaplastic thyroid carcinoma, multimodality therapy with resection, EBRT, and chemotherapy is preferred.

**Radiation Therapy Techniques**

- Simulation: supine, shoulder pulls, head and shoulder mask
  - Wire surgical scars
- Preoperative diagnostic imaging fused for treatment planning
- Full field IMRT will be used to target volumes
  - Alternative techniques include 3D-conformal planning.
- Postoperative dose is 60 Gy
  - 45 to 50 Gy to thyroid bed and nodal regions (levels II–IV, VI, superior mediastinal nodes)
  - Boost thyroid bed, central nodal compartment, and areas with involved nodes to 60 Gy
  - Escalate dose to 68 to 70 Gy if possible for gross residual disease

Organs at risk:
- Spinal cord: max 45 Gy
- Brachial plexus: max 66 Gy
- Parotids: combined mean less than 26 Gy, or mean less than 20 Gy in at least one gland
- Esophagus: mean less than 50 to 60 Gy
- Mandible: max 70 Gy

### 6.7 Unknown Head and Neck Primary Site

#### Epidemiology and Risk Factors

- Approximately 3% of head and neck squamous cell carcinomas metastasize to cervical lymph nodes from an unknown primary site
- Head and neck primary suspected for squamous cell carcinoma or poorly differentiated carcinoma
- Squamous cell carcinoma in the parotid is almost always metastatic from a cutaneous primary
- Adenocarcinoma almost always arises from a primary lesion below clavicles
- Risk factors
  - Depends on suspected primary site

#### Anatomy and Patterns of Spread

- For level IA involvement, likely primary sites include: mentum, middle 2/3 lower lip, anterior gingiva, and anterior tongue
- For level IB: ipsilateral lips, cheek, nose, medial canthus, oral cavity, and submandibular gland
- For level II: nasopharynx, oropharynx, oral cavity, larynx, hypopharynx, and parotid gland
- For level III: larynx, hypopharynx, thyroid, and infraclavicular primary
- For level IV: infraclavicular primary, thyroid, and esophagus
- For level V: nasopharynx
- For level VI: anterior cervical skin, larynx, and thyroid
- For parotid nodes: skin and oral cavity
- For bilateral nodes: nasopharynx, base of tongue, soft palate, pyriform sinus, and supraglottic larynx
- For Rouviere's node: nasopharynx and pharyngeal wall

#### Presentation

- Usually presents as an enlarging neck mass
- Often no obvious primary lesion is found
**Diagnosis and Workup**

- History and physical exam including complete head and neck exam with careful inspection and palpation of oral cavity and anterior oropharynx, examination of the skin of the head and neck region, fiberoptic nasopharyngolaryngoscopy, and palpation of all neck levels
- FNA of lymph node
  - Consider testing for HPV and EBV
- CT head/neck
- Consider MRI
- Chest x-ray
- PET/CT if above workup does not reveal primary
  - Should be performed prior to panendoscopy
- Panendoscopy with directed biopsies of nasopharynx, tonsil, base of tongue, piriform sinuses, and any suspicious lesions
  - Ipsilateral tonsillectomy recommended
- Routine laboratory studies
- Dental evaluation, nutrition evaluation, speech and swallowing evaluation, and audiology testing
  - Consider prophylactic feeding tube placement in patients receiving chemoradiation

**Stage**

- According to suspected primary site

**Treatment Overview**

- Primary treatment options include neck dissection or RT followed by evaluation for a neck dissection
- For single positive node without ECE, neck dissection alone is adequate
- For primary RT, include nasopharynx, oropharynx, and bilateral neck
  - Larynx and hypopharynx can be spared
  - Include oral cavity if level IB involvement
- Concurrent chemotherapy indicated for N2 and N3 disease
  - Preferred concurrent chemotherapy: cisplatin 100 mg/m² q21 days × 3 cycles
- For primary nonsurgically treated patients, follow with close follow-up (CT scan of neck 4 to 6 weeks after completion of RT to direct need for modified neck dissection)
  - Most patients with advanced N2–N3 disease should undergo a planned neck dissection as the likelihood of cure is low if a regional recurrence develops

**Radiation Therapy Techniques**

- Simulation: supine, shoulder pulls, head and shoulder mask
  - Wire lymph nodes, surgical scars
  - Bite block
  - Mouthguards
- Preoperative diagnostic imaging fused for treatment planning
- Full field simultaneous-integrated-boost IMRT will be used to target volumes:
  - Alternative techniques include split-field IMRT (match line just above arytenoids), sequential boost, brachytherapy boost, and 3D-conformal planning.
  - CTV generally includes pharyngeal axis including nasopharynx and oropharynx, and bilateral IB-V and retropharyngeal nodes.
- Dose (conventional fractionation):
  - Gross disease: ≥70 Gy
  - Mucosa: 50 to 60 Gy
  - High-risk nodal stations: 60 to 63 Gy
6.9 Eye/Orbit

Epidemiology and Risk Factors

- These are uncommon neoplasms, with approximately 2,500 cases annually in the United States.
- Most common malignancy is metastasis.
• Most common primary malignancies include ocular melanoma (eye) and orbital lymphoma (orbit).
  • Risk factors:
    o Uveal melanoma: light eye color, fair skin, UV light exposure, xeroderma pigmentosum, oculodermal melanocytosis, dyskastic nevus syndrome
    o Orbital lymphoma: same as for other non-Hodgkin's lymphomas

**Anatomy and Patterns of Spread**

• Ocular melanoma:
  o 80% arise in choroid; 10% to 15% in ciliary body; less than 10% in iris
  o Intraocular spread, including vitreous seeding
  o Extrascleral extension
  o Distant metastasis to liver greater than skin, lung

• Orbital lymphoma:
  o Arise in conjunctiva, lacrimal gland, eyelids, uvea, and intraconal and extracanal retrobulbar areas

**Presentation**

• Ocular melanoma: asymptomatic, visual field distortion, field loss, floaters, flashers, pain, glaucoma
• Orbital lymphoma: orbital mass, proptosis, diplopia, salmon, or flesh-pink colored lesion (conjunctiva)

**Histology**

• Ocular melanoma: spindle cell (grade 1), mixed cell (grade 2), and epithelioid cell (grade 3)
• Orbital lymphoma: extranodal marginal zone B-cell lymphoma or mucosa-associated lymphoid tissue (MALT)

**Diagnosis and Workup**

• History and physical
• Ocular melanoma: ultrasound, fundus photography, chest x-ray, liver function tests, CBC, LDH, CT chest/abdomen
• Orbital lymphoma: biopsy of lesion, bone marrow biopsy
• Collaborative Ocular Melanoma Study (COMS) classification:
  o Small: less than 3 mm thick; 5 to 16 mm largest dimension
  o Medium: 3 to 10 mm thick; 5 to 16 mm largest dimension
  o Large: greater than 10 mm thick; greater than 16 mm largest dimension
  o * Size in optic disc diameter: 1 dd = 1.5 mm

**Staging (AJCC 7th Edition Staging for Orbital Lymphoma)**

<table>
<thead>
<tr>
<th>T-stage</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Tx</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1a</td>
<td>Bulbar conjunctiva only</td>
</tr>
<tr>
<td>T1b</td>
<td>Palpebral conjunctiva ± fornix ± caruncle</td>
</tr>
<tr>
<td>T1c</td>
<td>Extensive conjunctival involvement</td>
</tr>
</tbody>
</table>

(continued)
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T-stage

<table>
<thead>
<tr>
<th>T2a</th>
<th>Anterior orbital involvement (± conjunctival involvement)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2b</td>
<td>Anterior orbital involvement (± conjunctival involvement + lacrimal involvement)</td>
</tr>
<tr>
<td>T2c</td>
<td>Posterior orbital involvement (± conjunctival involvement ± anterior involvement and ± any extraocular muscle involvement)</td>
</tr>
<tr>
<td>T2d</td>
<td>Nasolacrimal drainage system involvement (± conjunctival involvement but not including nasopharynx)</td>
</tr>
<tr>
<td>T3</td>
<td>Lymphoma with preseptal eyelid involvement (defined earlier) 16 ± orbital involvement ± any conjunctival involvement</td>
</tr>
<tr>
<td>T4a</td>
<td>Involvement of nasopharynx</td>
</tr>
<tr>
<td>T4b</td>
<td>Osseous involvement (including periosteum)</td>
</tr>
<tr>
<td>T4c</td>
<td>Involvement of maxillofacial, ethmoidal, and/or frontal sinuses</td>
</tr>
<tr>
<td>T4d</td>
<td>Intracranial spread</td>
</tr>
</tbody>
</table>

N-stage

| N0       | No evidence of lymph node involvement |
| N1       | Involvement of ipsilateral regional lymph nodes* |
| N2       | Involvement of contralateral or bilateral regional lymph nodes* |
| N3       | Involvement of peripheral lymph nodes not draining ocular adnexal region |
| N4       | Involvement of central lymph nodes |

M-stage

| M0       | No evidence of involvement of other extranodal sites |
| M1a      | Noncontiguous involvement of tissues or organs external to the ocular adnexa (e.g., parotid glands, submandibular gland, lung, liver, spleen, kidney, and breast) |
| M1b      | Lymphomatous involvement of the bone marrow |
| M1c      | Both M1a and M1b involvement |

*The regional lymph nodes include preauricular (parotid), submandibular, and cervical.

Treatment Overview

- Ocular melanoma:
  - Small
    - Observation
    - If growth: surgery, laser, plaque brachytherapy, proton RT or stereotactic radiosurgery
  - Medium
    - Surgery (enucleation, orbital exenteration, local resection + RT), RT (proton RT, helium, stereotactic radiosurgery, plaque brachytherapy)
  - Large
    - Enucleation
Orbital lymphoma:
- Low grade, limited disease: RT alone
- Intermediate-/high-grade disease: systemic therapy + RT
  - Systemic therapy is CHOP ± R

Toxicities:
- Acute: dermatitis, eye irritation
- Late: cataracts, retinopathy, glaucoma, dry eye

**Radiation Therapy Techniques**

Ocular melanoma:
- I-125 plaque brachytherapy:
  - Field: tumor + 2 mm margin
  - Plaque placed surgically, sutured in place, lead eye shield, 4 to 7 days treatment
  - I-125: minimum tumor dose 85 Gy; dose rate 0.6 to 1.05 Gy/hr
- Stereotactic radiosurgery:
  - 25 to 40 Gy single fraction to 50% isodose line

Orbital lymphoma:
- Radiation dose:
  - Low grade, limited disease: 30 to 30.6 Gy in 17 to 20 fractions
  - Intermediate-/high-grade disease: 40 Gy in 20 fractions
- Simulation:
  - Supine, head mask
  - Wire lateral canthus
  - Eye shield if tumor coverage is not compromised
  - Anterior lesions: 6 to 9 MeV electrons with 0.5 to 1.0 cm bolus
  - Lacrimal and intra- or extracanal involvement: 3DCRT or IMRT

**6.10 Nasal Cavity/Paranasal Sinuses**

**Epidemiology and Risk Factors**
- These are uncommon neoplasms, with approximately 4,500 new cases annually in the United States.
- 55% arise in maxillary sinus, 25% in ethmoid sinus, and 20% in nasal cavity.
- Risk factors:
  - Unclear. Possible chemical/occupational associations (sawmill workers/carpenters).

**Anatomy and Patterns of Spread**
- Nasal vestibule cancers may spread to nodes 15% of the time.
- Nasal vestibule typically drains to facial/buccinators nodes and submandibular nodes.
- Nasal cavity cancers in olfactory region drain to retropharyngeal nodes.
- Nasal cavity cancers in respiratory region rarely spread to nodes.
- Maxillary sinus cancers, if squamous or undifferentiated, have 30% nodal risk (submandibular, jugulodigastric, jugular, and retropharyngeal).
- Tumors superior–posterior to Ohngren's line (medial canthus to angle of mandible) have poorer prognosis.

**Presentation**
- Nasal vestibule: ulceration, crusting, scabbing, or minor bleeding
- Nasal cavity: nasal obstruction, discharge, or intermittent epistaxis
- Ethmoid sinus: sinus pain, nasal obstruction, proptosis, or diplopia
- Sphenoid sinus: headache, CN palsy (from cavernous sinus invasion), or retro-orbital pain

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• Maxillary sinus: sinus pain, oral cavity ulcer, ill-fitting dentures, nasal obstruction, epistaxis, trismus, headache, proptosis, or diplopia

**Histology**

• 80% are squamous cell carcinomas.
• Other histologies include sinonasal undifferentiated carcinoma (SNUC), sinonasal neuroendocrine carcinoma (SNEC), adenocarcinoma, rhabdomyosarcoma, lymphoma, plasmacytoma, melanoma, adenoid cystic carcinoma, and esthesioneuroblastoma (nasal cavity).

**Diagnosis and Workup**

• History and physical with thorough head and neck examination, including nasal endoscopy and palpation of all neck levels
• Biopsy
• CT head and neck
• Consider MRI skull base
• Consider PET/CT for stage III/IV disease
• Chest x-ray
• Routine laboratory studies

**Staging (AJCC 7th Edition)**

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>Tx</td>
<td>Primary tumor cannot be assessed</td>
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<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
</tbody>
</table>

**Maxillary Sinus**

- T1  Tumor limited to maxillary sinus mucosa with no erosion or destruction of bone
- T2  Tumor causing bone erosion or destruction including extension into the hard palate and/or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates
- T3  Tumor invades any of the following—bone of the posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa, ethmoid sinuses
- T4a Tumor invades anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid or frontal sinuses
- T4b Tumor invades any of the following orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V2), nasopharynx, or clivus

**Nasal Cavity and Ethmoid Sinus**

- T1  Tumor restricted to any one subsite, with or without bony invasion
- T2  Tumor invading two subsites in a single region or extending to involve an adjacent region within the nasoethmoidal complex, with or without bony invasion
- T3  Tumor extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribriform plate

(continued)
### T-stage

| T4a | Tumor invades any of the following anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses |
| T4b | Tumor invades any of the following orbital apex, dura, brain, middle cranial fossa, cranial nerves other than (V2), nasopharynx, or clivus |

### N-stage

| N0 | No regional lymph node metastasis |
| N1 | Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension |
| N2a | Metastasis in single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension |
| N2b | Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension |
| N2c | Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension |
| N3 | Metastasis in a lymph node more than 6 cm in greatest dimension |

### M-stage

| M0 | No distant metastases |
| M1 | Distant metastases |

### Group Stage

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<th>M</th>
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<tr>
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<td>Any N</td>
<td>M1</td>
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- **Kadish Staging System for Esthesioneuroblastoma**
  - Stage A: Tumor limited to nasal cavity
  - Stage B: Tumor involving the nasal cavity and paranasal sinuses
  - Stage C: Tumor extends beyond the nasal cavity and paranasal sinuses
  - Stage D: Lymph node or distant metastases
Treatment Overview

- Nasal cavity/ethmoid sinus
  - T1–2: Surgery + postoperative RT (except for T1) (preferred) or definitive RT
  - T3–4a: Surgery + postoperative RT (preferred) or definitive chemoradiation
  - T4b or unresectable: definitive chemoradiation
  - Notes:
    - Consider elective nodal treatment for squamous or undifferentiated tumors (extrapolating from maxillary sinus data).
    - If diagnosed incidentally upon resection of polyps, attempt re-excision to get negative margins.

- Maxillary sinus
  - T1–2N0 (except for adenoid cystic): surgery
    - Postoperative RT for PNI
  - T1–2N0 (adenoid cystic): surgery
    - Postoperative RT for suprastructure
  - T3–4N0: surgery + postoperative RT
  - T4b, Any N: definitive chemoradiation or radiation
  - T1–4aN+: surgery + postoperative RT
  - Notes:
    - Re-excision if possible for positive margins.
    - Systemic therapy is a component of care for SNUC.
    - Irradiate neck for T3–4a and node positive.
    - Preferred concurrent chemotherapy: cisplatin 100 mg/m² q21 days × 3 cycles.

Radiation Therapy Techniques

- Simulation
  - Supine, aquaplast, arms down in shoulder pulls, IV contrast, wire all scars, mark canthi. Fill surgical defects with water balloons if present.

- Preoperative diagnostic imaging fused for treatment planning.
- IMRT allows for more dose homogeneity and significantly reduces dose to the spinal cord, allowing for delivery of higher doses without added morbidity.

- Radiation volumes:
  - Include gross disease, remaining sinus, and portion of adjacent cavities/sinuses
  - Bilateral neck for greater than T2 esthesioneuroblastoma
  - Bilateral necks for T3–4 or node positive squamous cell carcinomas

- Radiation dose:
  - RT alone: 70 Gy in 35 fractions or altered fractionation
  - Chemoradiation: 70 Gy in 35 fractions
  - Postoperative radiation: 60 Gy conventionally fractionated

6.11 Ear

Epidemiology and Risk Factors

- Most ear cancers start on the skin of the outer ear.
- Primary cancers of the inner ear are rare.
- Risk factors:
  - Same as for other cutaneous squamous cell carcinomas
  - Chronic ear infections

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Anatomy and Patterns of Spread

- The ear comprises pinna, external auditory canal, tympanic membrane, and inner ear.
- Lymph node drainage is to parotid, cervical, and postauricular nodes.

Presentation

- Presenting symptoms depend on location of tumor.
  - External ear: persistent lesion
  - Middle ear: bloody discharge, hearing loss, earache
  - Inner ear: headache, hearing loss, tinnitus, dizziness

Histology

- Most are squamous cell carcinomas.
- Other histologies include: basal cell carcinoma, melanoma, and adenocarcinoma.

Diagnosis and Workup

- History and physical exam including complete skin exam, otoscopy, and palpation of regional nodal groups
- Biopsy
- CT head and neck
- Consider MRI
- Routine laboratory studies
- Chest x-ray
- Audiologic testing

Staging

- No site-specific AJCC staging. Use histology appropriate staging.

Treatment Overview

- External ear: primary surgery or RT
  - Surgery preferred for cartilage or auditory canal involvement.
  - Postoperative RT for close/positive margins, greater than 4 cm tumor, or cartilage invasion.
- Middle ear: primary surgery preferred
  - Postoperative RT in almost all cases given high risk of locoregional recurrence.
- Toxicities:
  - Hearing loss
  - Chronic otitis media
  - Cartilage or temporal bone necrosis

Radiation Therapy Techniques

- Simulation: supine, head and shoulder mask
- Use wax bolus to fill external auditory canal and around external ear to improve homogeneity.
- Pinna: orthovoltage x-rays or electrons
- External auditory canal/middle ear: 3D conformal or IMRT
  - Target volume should include ear canal and temporal bone with 2 to 3 cm margin, and ipsilateral preauricular, postauricular, and level II cervical lymph nodes.
- Dose:
  - Pinna: 50 to 60 Gy in 25 to 30 fractions
  - External auditory canal/middle ear: 66 to 70 Gy in 33 to 35 fractions (definitive); 60 Gy in 30 fractions (postoperative)
6.12 Skin—Nonmelanoma

Epidemiology and Risk Factors

- Basal and squamous cell carcinomas of the skin are the most common cancers in the United States with over 1 million new cases annually.
- Basal cell carcinoma is four times more common than squamous cell carcinoma.
- Risk factors:
  - Sun exposure
  - Chemical carcinogen exposure
  - Chronic irritation or inflammation
  - Ionizing radiation
  - Immunodeficiency
  - Genetic predisposition (xeroderma pigmentosum, basal cell nevus syndrome)

Anatomy and Patterns of Spread

- Basal cell carcinomas are generally slow growing over many years.
  - Spread to lymph nodes or distant organs is rare, less than 0.01%.
- Squamous cell carcinomas usually are more aggressive than basal cell carcinomas.
  - Incidence of regional metastasis at diagnosis is 2%; eventually 10% develop regional metastasis.
  - Prognosticators for spread include anatomic site, duration and size of the lesion, depth of dermal invasion, perineural invasion, and degree of differentiation.

Presentation

- Basal cell carcinomas most commonly present on the head and neck region, appearing as an asymptomatic nodule, pruritic plaque, or bleeding sore.
  - Variants include nodular-ulcerative, superficial, morphea-form, sclerosing, infiltrative, and terebrant

Histology

- Squamous cell carcinomas most commonly develop from skin exhibiting solar damage.
  - Less commonly, they arise from a thermal burn scar or chronic ulcer.
  - Actinic keratosis is a precursor of squamous cell carcinomas.
  - Variants include superficial, infiltrative, and spindle cell.

Diagnosis and Workup

- History and physical exam including complete skin exam and palpation of regional nodal groups
- Imaging studies obtained as indicated
- MRI for all patients in whom perineural spread is suspected
- Biopsy

Staging (AJCC 7th Edition Staging—Squamous Cell Carcinoma)

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</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
</tbody>
</table>

(continued)
Head and Neck Malignancies

T-stage

T1  Tumor 2 cm or less in greatest dimension with less than two high-risk features

T2  Tumor greater than 2 cm in greatest dimension or tumor any size with two or more high-risk features

T3  Tumor with invasion of maxilla, orbit, or temporal bone

T4  Tumor with invasion of skeleton (axial or appendicular) or perineural invasion of skull base

N-stage

N0  No regional lymph node metastasis

N1  Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension

N2a Metastasis in single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension

N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension

N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension

N3  Metastasis in a lymph node more than 6 cm in greatest dimension

M-stage

M0  No distant metastases

M1  Distant metastases

*High-Risk Features for the Primary Tumor (T) Staging:

- Depth/Invasion: greater than 2 mm thickness, Clark level IV, Perineural invasion
- Anatomic Location: Primary site ear, Primary site hair-bearing lip
- Differentiation: Poorly differentiated or undifferentiated

<table>
<thead>
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<th>Group Stage</th>
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<th>M</th>
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<tbody>
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<tr>
<td></td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
Treatment Overview

- Primary treatment is wide excision with negative margins.
- If clinically lymph node positive, regional lymph node dissection recommended.
- Primary RT given for nonsurgical patients.
- Adjuvant RT recommended for node positive disease, greater than 3 cm primary, perineural invasion, bone/cartilage/muscle invasion, and recurrent disease.
- Adjuvant chemoradiation recommended for positive margins or extracapsular extension.
- A hedgehog pathway inhibitor should be considered for unresectable basal cell carcinomas.

Radiation Therapy Techniques

- Simulation depends on location.
- Superficial/orthovoltage x-rays and electrons are most commonly used.
- Tissue equivalent bolus is used for adequate skin surface dose.
- Use eye shields as needed to protect lens.
- Use wax-covered lead shield as needed to shield teeth, mandible, and nasal cavity.
- Protracted fractionation is associated with improved cosmetic results.
- Primary RT:
  - Less than 2 cm: 64 Gy in 32 fractions; 55 Gy in 20 fractions; 50 Gy in 15 fractions; 35 Gy in 5 fractions.
  - Greater than 2 cm: 66 Gy in 33 fractions; 55 Gy in 20 fractions.
- Adjuvant RT: 50 Gy in 20 fractions; 60 Gy in 30 fractions.
- Primary regional nodal RT: 66 to 70 Gy in 2 33 to 35 fractions.
- Adjuvant regional nodal RT: 56 to 66 Gy in 28 to 33 fractions.

6.13 Skin—Melanoma

Epidemiology and Risk Factors

- There are 76,000 cases annually in the United States. Incidence continues to rise.
- Median age at diagnosis is 59 years.
- Risk factors:
  - History of melanoma, atypical moles, or dysplastic nevi
  - Rarely, familial susceptibility
  - Fair skin and an inability to tan.

Anatomy and Patterns of Spread

- 85% present with localized disease, 10% present with regional disease, and 5% present with metastatic disease.
- Nodal involvement is the strongest prognostic factor.

Presentation

- Typically present with suspicious pigmented lesion

Diagnosis and Workup

- History and physical exam including complete skin exam and palpation of regional nodal groups
- Excisional biopsy of primary with 1 to 3 mm margins to make diagnosis
  - If excisional biopsy not feasible, then full thickness punch biopsy of thickest part is reasonable
- Assessing pathology with Breslow thickness, mitotic rate, and ulceration best predict risk of lymph node metastases
• Sentinel lymph node biopsy:
  o Need not be offered to stage IA patients without adverse features.
  o Indicated for tumor thickness of 0.75 to 1 mm and adverse features such as young age, ulceration, high
    mitotic rate, positive deep margin can be considered.
  o Note: pure desmoplastic melanomas that have been confirmed as such by dermatopathologist have very
    low incidence of LN metastases. SLN biopsy is contraindicated in these patients.
• Patients with a positive sentinel node or clinically positive nodes should be considered for nodal dissection.

Stage (AJCC 7th Edition)

<table>
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<td>T1a</td>
<td>Without ulceration and mitosis &lt;1/mm²</td>
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<tr>
<td>T1b</td>
<td>With ulceration or mitoses &gt; 1/mm²</td>
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<tr>
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<td>N2b</td>
<td>Macrometastasis†</td>
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<tr>
<td>N2c</td>
<td>In transit met(s)/satellite(s) without metastatic nodes</td>
</tr>
</tbody>
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## N-stage

| N3 | Clinical: ≥ 1 node with in transit met(s)/satellite(s); Pathologic: 4 or more metastatic nodes, or matted nodes, or in transit met(s)/satellite(s) with metastatic node(s) |

## M-stage

| M0 | No distant metastases |
| M1a | Metastases to skin, subcutaneous tissues, or distant lymph nodes |
| M1b | Metastases to lung |
| M1c | Metastases to all other visceral sites or distant metastases to any site combined with an elevated serum LDH |

*Micrometastases are diagnosed after sentinel lymph node biopsy and completion lymphadenectomy (if performed).
†Macrometastases are defined as clinically detectable nodal metastases confirmed by therapeutic lymphadenectomy or when nodal metastasis exhibits gross extracapsular extension.

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<tbody>
<tr>
<td></td>
<td>T1–4a</td>
<td>N1b</td>
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<tr>
<td></td>
<td>T1–4a</td>
<td>N2b</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1–4a</td>
<td>N2c</td>
<td>M0</td>
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<tr>
<td>nIIIC</td>
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<td></td>
<td>T1–4b</td>
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<td>M0</td>
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<tr>
<td></td>
<td>T1–4b</td>
<td>N2c</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
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**Treatment Overview**

- Primary treatment is wide excision with or without sentinel node biopsy (see prior section for sentinel lymph node biopsy).

<table>
<thead>
<tr>
<th>Tumor Thickness</th>
<th>Recommended Clinical Margins</th>
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<tbody>
<tr>
<td>In situ</td>
<td>0.5–1.0 cm</td>
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<tr>
<td>≤1.0 mm</td>
<td>1.0 cm</td>
</tr>
<tr>
<td>1.01–2 mm</td>
<td>1–2 cm</td>
</tr>
<tr>
<td>2.01–4 mm</td>
<td>2 cm</td>
</tr>
<tr>
<td>&gt;4 mm</td>
<td>2 cm</td>
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- Adjuvant RT is given in select settings.
- Treatment of the primary site with RT is not typically necessary.
  - Exception is desmoplastic variant with neurotropism. Consider adjuvant treatment in this histology, particularly if margins are questionable.
- Nodal basin irradiation improves locoregional control but not overall survival.
  - Locoregional failure rates after resection and RT are 5% to 10%.
  - Consider adjuvant RT to nodal sites for
    - ≥1 involved parotid node, any size of involvement
    - ≥2 involved cervical nodes or ≥3 cm tumor within a node
    - ≥2 involved axillary nodes or ≥4 cm tumor within a node
    - ≥3 involved inguinal nodes or ≥4 cm tumor within a node
    - Any ECE
    - In groin consider strongly giving only RT for two of these risk factors if BMI greater than 25.
- In stages IIB and IIC, offer interferon alpha or clinical trial.
- In stage III, offer clinical trial.
- In stage IV, offer systemic therapy including Ipilimumab, Vemurafenib, Dabrafenib, or high-dose IL-2, or clinical trial.
- Consider palliative resection or RT for symptomatic disease.
  - Toxicity:
    - Dermatitis, hematopoetic suppression, but most worrisome lymphedema.
    - Risk of complications significantly related to BMI:
      - BMI of 25 to 30 or greater associated with increased risk.
    - Risk of lymphedema from cervical RT is low.
    - Axillary grade 3 to 4 lymphedema occurred in 8% of TROG patients and the rate of clinically significant edema was 42%.
    - Inguinal lymphedema much more common, with estimates at 4 years of 30% to 50% of grade 3.

**Radiation Therapy Techniques**

- Simulation depends on location
  - Open neck position for neck
  - Akimbo for axilla
  - Frog legged for inguinal
- Dose: 30 Gy in five fractions biweekly
- Organs at risk:
  - Limit brain, spinal cord, and bowel to less than 24 Gy.

### 6.14 Salivary Gland

**Epidemiology and Risk Factors**

- There are approximately 2,500 new cases annually in the United States.
- Incidence is equivalent in males and females.
- Average age at diagnosis is 55 years.
- Salivary glands are composed of two main groups: major and minor.
  - Major salivary glands include parotid, submandibular, and sublingual.
  - Minor salivary glands line the mucosa of the upper aerodigestive tract, with common sites including the hard palate, buccal mucosa, oropharynx, nasal cavity, and paranasal sinuses.
- Parotid gland cancers account for 80% to 90% of all malignant salivary gland tumors.
- 15% to 30% of parotid gland tumors are malignant.
- 50% of submandibular gland tumors are malignant.
- 80% of sublingual gland tumors are malignant.
- The majority of minor salivary gland tumors are malignant.
- Suggested risk factors: nutritional deficiencies (vitamins A and C), exposure to ionizing radiation, UV exposure, genetic predisposition, history of previous cancer of the skin of the face, occupational exposure, viral infection (EBV), and alcohol use.

**Anatomy and Patterns of Spread**

- Parotid gland is divided into deep and superficial lobes by the facial nerve.
- Parotid glands drain into oral cavity via Stensen's duct.
- Submandibular glands drain into oral cavity via Wharton's duct.
- Sublingual glands drain into oral cavity via Bartholin's duct.
- Most common pattern of spread is by local infiltration and perineural extension.
- Hematogenous spread is more common than regional lymph node metastases:
  - Distant metastases most commonly involve lungs, bones, and liver.
  - Adenoid cystic carcinomas metastasize distantly in approximately 50% cases.
  - Minor salivary gland cancers metastasize distantly in approximately 25% cases.
Lymph node metastases vary depending on histology, T-stage, site of origin, and grade.

Lymphatic drainage:
- Parotid gland: intraparotid, I to III.
- Submandibular gland: I to III.
- Sublingual gland: I to III.

**Presentation**

- Signs and symptoms:
  - Malignant parotid cancers: painless, rapidly enlarging mass; facial weakness, pain, numbness, cranial neuropathy
  - Submandibular gland cancers: mildly tender mass; cranial nerve V, VII ( marginal branch), and XII involvement (advanced lesions)
  - Minor salivary gland cancers: symptoms dependent on site of origin

**Histology**

- Classification of malignant salivary gland tumors:
  - Carcinoma ex pleomorphic adenoma
  - Adenoid cystic carcinoma
  - Mucoepidermoid carcinoma
  - Adenocarcinoma (NOS)
  - Acinic cell carcinoma
  - Squamous cell carcinoma
  - Myoepithelial carcinoma
  - Cystadenocarcinoma
  - Small cell carcinoma
  - Polymorphous low-grade adenocarcinoma
  - Epithelial myoepithelial carcinoma
  - Clear cell carcinoma (NOS)
  - Basal cell adenocarcinoma
  - Salivary duct carcinoma
  - Carcinoma-sarcoma
  - Metastasizing pleomorphic adenoma
  - Large cell undifferentiated carcinoma
  - Lymphoepithelial carcinoma
  - Other rare histologies

**Diagnosis and Workup**

- History and physical exam including complete head and neck exam including palpation of all neck level and thorough cranial nerve exam
- FNA biopsy of mass
  - Avoid incisional or excisional biopsy because it is associated with higher rate of local recurrence
- CT head and neck and MRI head and neck can be complementary in evaluating tumor depth and local extension
- Chest x-ray
- PET for high-grade aggressive lesions
- Routine laboratory studies
- Dental evaluation, nutrition evaluation, speech and swallowing evaluation, and audiology testing
  - Consider prophylactic feeding tube placement in patients receiving chemoradiation
**Staging (AJCC 7th Edition)**

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Description</th>
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<tr>
<td>Tx</td>
<td>Primary tumor cannot be assessed</td>
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<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
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<td>T1</td>
<td>Tumor 2 cm or less in greatest dimension without extraparenchymal extension</td>
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<tr>
<td>T2</td>
<td>Tumor more than 2 cm but not more than 4 cm in greatest dimension without extraparenchymal extension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor more than 4 cm and/or tumor having extraparenchymal extension</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor invades skin, mandible, ear canal, and/or facial nerve</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades skull base and/or pterygoid plates and/or encases carotid artery</td>
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<td>Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension</td>
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<tr>
<td>N2a</td>
<td>Metastasis in single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N2b</td>
<td>Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N2c</td>
<td>Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in a lymph node more than 6 cm in greatest dimension</td>
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<td>Distant metastases</td>
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<td>N2</td>
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(continued)
### Treatment Overview

- Primary treatment is surgical resection.
  - Exceptions include medically inoperable patients, patients who refuse surgery, distant metastases, unresectable cancers, cancers in which surgical resection would result in significant and unacceptable functional or cosmetic deficits.
- Parotid cancers are typically resected by superficial parotidectomy.
- Deep lobe removal depends on location, extent, and histology.
- Facial nerve is generally preserved unless nerve is grossly encased or involved with cancer.
- Neck dissection indicated for palpable adenopathy or a high-grade primary cancer with aggressive histologic features and high risk of subclinical nodal metastases.
- Primary RT (high-dose conventional EBRT, brachytherapy, neutron beam therapy) can be used for unresectable cancers or for palliation.
- No clear role for chemotherapy in definitive setting.
- Indications for postoperative RT: close/positive margins, high-grade cancer, involvement of skin or bone, involvement of nerve (gross invasion or extensive PNI), tumor extension beyond capsule of gland, lymph node metastases, large tumors requiring radical resection, tumor spillage, recurrent cancer.
- For patients with large primary cancer, high-grade cancer, high-risk histologic features (small cell carcinoma, malignant mixed tumors, mucoepidermoid carcinoma, adenocarcinoma), or high-risk (lymphatic rich) primary tumor site, elective neck dissection or elective neck irradiation is indicated.
- Consider palliative resection or RT for symptomatic disease.

### Radiation Therapy Techniques

- Simulation: supine, shoulder pulls, head and shoulder mask
  - Wire lymph nodes, surgical scars, oral commissure
  - Bite block
  - Mouthguards
- Preoperative diagnostic imaging fused for treatment planning
- IMRT is favored for improved homogeneity and reduced dose to contralateral critical structures.
  - Other options include wedge pair or mixed photon/electrons
- Treat primary tumor bed alone for low grade, node-negative patients.
- Consider elective neck RT for high-grade clinically node-negative tumors.
- Treat entire ipsilateral neck RT for node-positive tumors.
- For extensive nerve invasion or adenoid cystic histology, cover nerve pathway up to the base of the skull.
- Radiation dose:
  - Postoperative dose is 60 Gy standard fractionation; consider boost when indicated.
  - Elective neck irradiation dose is 50 to 54 Gy standard fractionation.
  - Definitive dose is at least 66 Gy.

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<table>
<thead>
<tr>
<th>Group Stage</th>
<th>T</th>
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<td>T4b</td>
<td>Any N</td>
<td>M0</td>
</tr>
<tr>
<td>IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
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</table>
- Organs at risk:
  - Spinal cord: max 45 Gy
  - Brainstem: max 54 Gy
  - Optic chiasm and nerves: max 54 Gy
  - Temporal brain: max 60 Gy
  - Mandible: max 70 Gy

**Chapter 6: Practice Questions**

1. Subglottic cancers are what percentage of all larynx cancers?
   - A. <5%
   - B. 10%
   - C. 15%
   - D. 20%

2. The primary indication for the use of concurrent chemoradiation for unknown head and neck primary cancer is
   - A. Large primary cancer
   - B. Primary tumor site
   - C. Nodal status
   - D. Tumor grade

3. The most frequent site of oral cavity cancer is located at
   - A. Lips
   - B. Tongue
   - C. Floor of mouth
   - D. Hard palate

4. Cancer of the inner ear is usually associated with the following signs/symptoms EXCEPT
   - A. Bloody discharge
   - B. Headache
   - C. Hearing loss
   - D. Tinnitus

5. Bilateral nodal metastases from nasopharyngeal cancer no greater than 2 cm is N staged as
   - A. N1
   - B. N2
   - C. N3a
   - D. N3b

6. Which of the following tumors can present with cranial nerve palsies?
   - A. Ethmoid sinus
   - B. Sphenoid sinus
   - C. Maxillary sinus
   - D. Nasal cavity

7. Any skin cancer with orbital involvement is T staged as
   - A. T3
   - B. T4
   - C. T4a
   - D. T4b
8. Indications for postoperative head and neck radiation include the following EXCEPT
   A. Multiple node positivity
   B. Large nodal size
   C. Extracapsular extension
   D. Tumor grade

9. All these subtypes of oropharynx cancer have a 70% risk of nodal involvement EXCEPT
   A. Soft palate
   B. Base of tongue
   C. Tonsillar pillar
   D. Tonsillar fossa

10. The nodal drainage of the ear is usually to all of the following EXCEPT
    A. Parotid nodes
    B. Cervical nodes
    C. Postauricular nodes
    D. Scalene nodes

11. Nasal cavity tumors that invade the frontal sinuses are best T staged as
    A. T3
    B. T4
    C. T4a
    D. T4b

12. The following are all risk factors for lymphatic spread of oral cavity cancer EXCEPT
    A. Depth of invasion
    B. Primary tumor site
    C. T stage
    D. Grade

13. The least frequently seen subtype of thyroid cancer is
    A. Anaplastic
    B. Medullary
    C. Follicular
    D. Papillary

14. A typical dose for areas of ECE or positive margin in the context of postoperative radiation in oropharynx cancer is
    A. 54 Gy
    B. 57 Gy
    C. 60 Gy
    D. 66 Gy

15. All of the following are associated with the development of thyroid cancer EXCEPT
    A. Radiation exposure
    B. MEN-1 syndrome
    C. Cowden's syndrome
    D. Gardner's syndrome

16. The most frequent histology associated with cancer of the ear is
    A. Basal cell carcinoma
    B. Melanoma
    C. Adenocarcinoma
    D. Squamous cell carcinoma
17. A CTV54 for postoperative head and neck radiation is usually used to
   A. Cover the high-risk tumor bed
   B. Cover the entire operative bed
   C. Cover the involved nodal areas
   D. Cover surgically undisturbed sites at microscopic risk of disease

18. The usual recommended time to start postoperative RT after head and neck surgery is generally
   A. Within a week of surgery
   B. 2 to 3 weeks
   C. 4 to 6 weeks
   D. 8 to 12 weeks

19. All of the following are typical dose fractionation schedules for T1 or T2 radical intent larynx cancer EXCEPT
   A. 66 Gy in 33 fractions
   B. 70 Gy in 35 fractions
   C. 63 Gy in 28 fractions
   D. 60 Gy in 30 fractions

20. Submandibular glands drain into the oral cavity through
   A. Stensen's duct
   B. Wharton's duct
   C. Barholin's duct
   D. Cuvier duct
Chapter 6: Answers

1. A
2/3 of larynx cancers are glottic, 1/3 are supraglottic, and 2% are subglottic.

2. C
Concurrent chemotherapy indicated for N2 and N3 unknown primary head and neck cancer. Preferred concurrent chemotherapy: cisplatin 100 mg/m² q21 days × 3 cycles.

3. A
Distribution of oral cancers by subsite:
- Lips: 45%
- Oral tongue: 16%
- Floor of mouth: 12%
- Alveolar ridge: 12%
- Buccal mucosa: 10%
- Hard palate: 5%

4. A
Presenting symptoms for cancer of the ear depend on location of tumor:
- External ear: persistent lesion.
- Middle ear: bloody discharge, hearing loss, earache.
- Inner ear: headache, hearing loss, tinnitus, dizziness.

5. B
N staging of nasopharynx:
- N1: Unilateral metastasis in lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa, and/or unilateral or bilateral, retropharyngeal lymph nodes, 6 cm or less, in greatest dimension
- N2: Bilateral metastasis in lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa
- N3: Metastasis in a lymph node(s) greater than 6 cm and/or extension to supraclavicular fossa
  - N3a: Greater than 6 cm in dimension
  - N3b: Extension to the supraclavicular fossa

6. B
The presentation of sphenoid sinus cancer can include the following:
- Headache
- CN palsy (from cavernous sinus invasion)
- Retro-orbital pain

7. A
T staging of locally advanced skin cancers:
- T3: Tumor with invasion of maxilla, orbit, or temporal bone
- T4: Tumor with invasion of skeleton (axial or appendicular) or perineural invasion of skull base

8. D
Indications for postoperative RT include:
- Advanced stage (T3-T4)
- Positive or close surgical margins
- Lymphovascular invasion
- Perineural invasion
- Greater than one positive node
- Any single positive node greater than 3 cm
- Extracapsular extension

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9. A
Clinical nodal involvement at diagnosis
   - BOT: 75%
   - Tonsillar fossa: 75%
   - Tonsillar pillar: 45%
   - Soft palate: 45%
   - Oropharyngeal wall: 70%

10. D
Anatomy and patterns of spread of cancer of the ear:
    - The ear is comprised of pinna, external auditory canal, tympanic membrane, and inner ear.
    - Lymph node drainage is to parotid, cervical, and postauricular nodes.

11. C
T staging of advanced nasal cavity tumors:
   - T3: Tumor extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribriform plate
   - T4a: Tumor invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses
   - T4b: Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than (V2), nasopharynx, or clivus

12. B
Increasing depth of invasion, T-stage, and grade are associated with greater risk of lymph node involvement. Tumor site is associated with nodal levels at risk:
   - Upper lip: facial and level IB
   - Lower lip: I–III
   - Floor of mouth: I–III
   - Buccal mucosa: I–III
   - Alveolar ridge: levels I–III
   - Oral tongue: I–IV

13. A
Pathology of thyroid cancer:
   - Papillary thyroid cancer accounts for 40% to 90% cases, usually younger women.
   - Follicular thyroid cancer (includes oxyphilic or Hurthle cell variants) accounts for 15% to 40% cases
   - Medullary thyroid cancer accounts for 2% to 8% cases
   - Anaplastic thyroid cancer accounts for 1% to 5% cases

14. D
Postoperative RT for oropharynx cancer:
   - 60 Gy to tumor bed + approximately 1 cm margin
   - 57 Gy to entire primary operative bed and involved neck nodal levels
   - 54 Gy to intermediate-risk areas outside of operative bed and elective neck
   - Consider 66 Gy for areas at very high risk (ECE, positive margin)

15. B
Risk factors for thyroid cancer development:
   - Prior ionizing radiation exposure
   - Dietary iodine content
   - Family history of thyroid cancer
   - Multiple endocrine neoplasia type 2 (MEN-2)—medullary thyroid cancer
   - Cowden's syndrome—papillary thyroid cancer
   - Gardner's syndrome—papillary thyroid cancer
16. D
Most cancers of the ear are squamous cell carcinomas. Other histologies include: basal cell carcinoma, melanoma, and adenocarcinoma.

17. D
Postoperative head and neck radiation:
CTV60 will include tumor bed + ~1 cm margin. Include surgical clips, scar.
CTV57 will include CTV60 + entire primary operative bed and involved neck nodal levels.
CTV54 will include CTV60 as well as surgically undisturbed sites at risk for microscopic disease.

18. C
Postoperative RT should begin within 4 to 6 weeks of surgery. Locoregional control and overall survival better with early RT.

19. D
Dose fractionation schedules for larynx cancer:
T1: 66 Gy in 33 fractions or 63 Gy in 28 fractions
T2: 70 Gy in 35 fractions (6 fractions per week) or 65.25 Gy in 29 fractions

20. B
Parotid glands drain into oral cavity via Stensen's duct. Submandibular glands drain into oral cavity via Wharton's duct. Sublingual glands drain into oral cavity via Bartholin's duct.

Recommended Reading


